REMARKS

Claims 1-30 were pending in this application prior to this response. By the present response claims 1, 3, 4, 11, 12, 15, 16, 17, 18, 20, 21, 23, 24, 25, 26, 27 have been amended to define Applicants' invention with greater particularity. For example, support for "thermal decomposition or microfluidic impregnation," as provided in claim 20, can be found at paragraph [0010] and in Figure 4 of the specification. Support for "microfluidic impregnation" can be found beginning at paragraph [0042] . Support for "thermal annealing," as provided in claim 25, can be found in Example 2, beginning at paragraph [0074]. Support for "chamber or trench," as provided in new claim 31, can be found at paragraph [0033]. Support for "nanoparticle aggregates or cross-linked nanoparticles," as provided in claim 32, can be found at paragraph [0048]. The new claim language adds no new matter, being fully supported by the Specification and original claims. Accordingly claims 1-32 are currently pending.

The Rejection under 35 U.S.C. § 102(b)

Claims 1-10, 13-18 and 21-30 stand rejected as allegedly anticipated by Schlottig et al. (WO 00/08445; hereinafter "Schlottig"). Applicants traverse this rejection as it may apply to the amended claims.

The invention methods, as defined by amended claim 1, distinguish over the disclosure of Schlottig by requiring "providing a porous substrate comprising a metal-coated contact surface, wherein the contact surface comprises one or more capture molecules; contacting the surface with a sample comprising one or more analytes; and using laser excitation and spectroscopy to detect and/or identify one or more analytes bound to a capture molecule." With regard to the invention apparatus defined by amended claim 15, Applicants submit that Schlottig is distinguished by requiring "a nanocrystalline porous substrate comprising a metal-coated contact surface, wherein the contact surface comprises one or more capture molecules; a laser, a Raman detector, and a spectrometer." Similarly, Applicants submit that the invention wafer, as defined by amended claim 23, distinguishes over Schlottig by requiring "a layer of nanocrystalline porous silicon, the layer comprising a metal-coated surface."

To establish anticipation under 35 U.S.C. § 102(b) requires that the reference disclose each and every element of the claims at issue. As noted above, Schlottig fails to disclose each and every element of the claims as currently amended and, hence, fails to anticipate claims 1-10, 13-18 and 21-30. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The Rejections under 35 U.S.C. § 103

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Claims 11-12 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schlottig (as above) in view of Natan (U.S. publication 2002/0142480). The remarks above concerning the failure of Schlottig to anticipate the invention methods and apparatus apply equally and are incorporated here. In addition, Applicants submit that Schlottig fails to suggest the invention methods of claims 11 and 12 (which depend from claim 1) because Schlottig is absolutely silent regarding use of a porous substrate comprising a metal-coated contact surface that includes one or more capture molecules, such as one having at least one chamber or trench formed therein in the micrometer size range in a method for capture and spectroscopic analysis of, for example, single nucleotides. In fact, Schlottig's invention is based on the theory that "the entity of nanobodies must have an optimal size distribution" to enhance interaction with the substance which is adsorbed on the substrate surface. Thus, Schlottig discloses only pores formed by regimented protrusions from the upper surface of a substrate base, wherein only 3-5% variance in the height of these "nanobodies" is preferred (Schlottig, page 4, lines 20-23). Schlottig's first making a mold with orthogonal depressions and then casting the substrate into the mold, which is then removed, assures such regularity of the protrusions. Schlottig's disclosure is unsuitable for use in detection of a single nucleotide because it is designed to overcome the shortcomings of a randomly roughened surface for the metal-covered substrate.

The Examiner relies upon Natan as disclosing "attach[ment of] capture molecules, such as ligands to nanoparticles" (Office Action, page 5), but Applicants submit that Natan fails to disclose or suggest the invention method of using "porous substrate with a metal covering the contact surface", as required in the invention methods because Natan's disclosure concerns "free standing" nanoparticles, which "sandwich" a Raman-active material having a thickness as small as one molecule between stripes of metal (SSNs). Natan does not contemplate use of the "free standing" SSNs with any type of substrate. Thus, Natan fails to overcome the deficiencies of Schlottig for suggesting the invention methods.

Moreover Applicants submit that nothing in Natan suggests modification of Schlottig's methods by use of a porous substrate because Natan's SSN's are designed as "tags" to be used in the same way that a fluorescent molecule is used (i.e., by direct attachment to an analyte in all types of different assays, suggesting no need for a porous substrate, such as a crystalline or nanocrystalline substrate.

Accordingly, Applicants submit that *prima facie* obviousness of claims 11 and 12 under 35 U.S.C. 103(a) is not established by the combined disclosures of Schlottig and Natan. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Applicants also respectfully traverse the rejection of claim 19 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schlottig (as above) in view of Carraba. The remarks above concerning the failure of Schlottig to anticipate the invention apparatus of claim 15 apply equally and are incorporated here. In addition, Applicants submit that Schlottig fails to suggest the invention apparatus of claim 19 (which depends from claim 15) because Schlottig is absolutely silent regarding an apparatus comprising a *nanocrystalline* porous substrate having an upper surface coated with a metal together with a laser and a Raman detector. In fact, as Applicants point out above, Schlottig discloses only a porous substrate with pores formed by regular orthogonal protrusion from a substrate and the substrate is made by first making a mold with depressions and then casting the substrate into the mold, which is then removed. Nothing in Schlottig's disclosure suggests use of crystalline substrate into which the "roughened surface" necessary for SERS is formed by etching, and the like. In fact, Schlottig's invention is meant to be an improvement over such structures. Therefore, Applicant respectfully submits that the knowledge of the art regarding use of computers in systems used for SERS spectroscopy does not overcome this deficit in Schlottig for suggesting the invention apparatus as defined by claim 19.

In addition, Applicants respectfully traverse the rejection of claim 20 under 35 U.S.C. § 103 as allegedly being unpatentable over Schlottig (as above) in view of Carrabba et al. (U. S. Patent No. 5,255,067; hereinafter "Carrabba"). The Examiner acknowledges: "Schlottig does not disclose a flow through cell operably coupled to the Raman detector, wherein flow passes through the substrate inside the flow through cell" (Office Action, page 5). Applicants disagree with the Examiner's assertion that that Carrabba describes an apparatus in which the flow is "through the substrate" (Office Action, page 6). Instead, in Carrabba's apparatus (See Fig. 7) the flow through cell 30 "contains" the substrate, exposing a flow of gas only to the contact adsorptive surface of a bilayer substrate. The adsorbing or reactive layer in the substrate that contact the gas is composed of such substances as an oxide, such as a metal oxide, a compound that interacts with gas species, such as high surface area carbon, hydrated silica, or zeolite molecular sieves (Col. 5 lines 10-25), or a conductive polymer (Col 6, lines 37-46). The Raman-active metal surface lies under the adsorptive layer and does not directly contact the gas molecules. Thus, Carrabba is absolutely silent regarding a porous nanocrystalline substrate with a metal-coated contact surface, let alone an apparatus in which the flow through cell is sized to be contained within the substrate (e.g., a nanotube). Carrabba is also silent with regard to producing the substrate by a method that includes thermal decomposition or microfluidic impregnation of a metal salt, as provided in amended claim 20.

Accordingly, Applicants submit that there is no motivation in the combined disclosures of Schlottig and Carrabba to locate the flow through cell inside a nanocrystalline substrate with a metal coating because neither Schlottig nor Carrabba discloses crystalline substrates at all, and even if those of skill in the art were motivated by the combined disclosures of Schlottig and Carrabba to arrive at Applicants' invention apparatus of claim 20, there would be no reasonable expectation of success based on the disclosure of the cited art.

Therefore, Applicant respectfully submits that prima facie obviousness of claim 20 under 35 U.S.C. § 103 is not established by the combination of Schlottig and Carrabba and reconsideration and withdrawal of the rejection are respectfully requested.

The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application. The Commissioner is authorized to charge any additional fees that may be required, or credit any overpayments, to Deposit Acct. No. 50-1355.

Respectfully submitted,

Lisa Haile

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Lisa A. Haile, J.D., Ph.D.
Reg. No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
ATTORNEYS FOR INTEL CORPORATION
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
Customer Number: 28213